

REMARKS

Responsive to the Office Action mailed August 17, 2010, Applicants respectfully request entry of these amendments and remarks and respectfully request reconsideration and allowance of the application.

Status of the claims

Claims 1-26 were pending as of the August 17th mailing date of the Office Action. Claims 3, 4, 7, 8, 22, and 23 are withdrawn by the Office.

Claims 1, 2, 5, 6, 9-21, and 24-26 stand rejected under 35 U.S.C. § 101 as allegedly directed to nonstatutory subject matter.

Claims 1, 2, 5, 6, 9, 10, 13-15, 17-21, 24, and 25 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Ooi et al., Bioinformatics vol. 19 no. 1 pp. 37-44 (2003) (hereinafter "Ooi") in view of Chtioui et al., J. Sci. Food Agric. (1998) (hereinafter "Chtioui").

Claims 11, 12, and 26 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Ooi in view of Chtioui in further view of Liu et al., Evolutionary Computation, 12-17 May, pp. 297-302 (2002) (hereinafter "Liu").

Claims 12 and 13 are objected to for cited informalities.

Comment on the Restriction

Applicants again traverse the restriction, for reasons set forth previously. Moreover, the articulation of the finality of the restriction is based on PCT rules governing unity of invention. Office Action pages 2-4. It is respectfully submitted that any final restriction should be based on U.S. restriction rules.

Applicants again urge reconsideration and withdrawal of the restriction notwithstanding its finality.

**The claims present patentable subject matter, meet all statutory requirements,
and should be allowed**

The objections to claims 12 and 13 are remediated as suggested at Office Action page 5. Applicants urge these objections be withdrawn in view of these amendments.

The § 101 rejections are remediated as follows. Claim 1 is amended to recite the computational genetic evolving being performed by a computing system. Claim 15 is amended to recite computationally genetically evolving the genes of the chromosomes using a computing system. Each of claim 19 and claim 21 is amended to recite the computational genetic evolving and the selecting are performed by a computing system. These amendments find support in the original specification at least in optimization system (8) implementing the disclosed computational algorithms.

Dependent claims 13, 18, and 20 are amended to recite classifying ... using a classifier ... implemented by a computer. These amendments find support in the original specification at least in processing elements 62, 64, 66 which are disclosed as being suitably embodied by a computer. *See* application page 9 lines 6-15.

With these amendments, all claims recite a machine performing method operations constituting significant activity (e.g., at least the computational genetic evolving operations), and thus are respectfully submitted to satisfy the *Bilski* machine-or-transformation test. Accordingly, Applicants urge the § 101 rejections be reconsidered and withdrawn in view of these amendments.

The § 103 rejections are respectfully traversed as followed.

Claim 1 is amended to recite a set of genes specifying a sub-set of an associated set of measurements wherein each gene of the set of genes contains an index value which indexes a measurement of the associated set of measurements. This amendment finds support in the original specification at least at page 7 lines 5-17.

Claims 1 is rejected as allegedly obvious in view of the proposed combination of Ooi and Chtioui. The Office Action recognizes Ooi does not disclose or fairly suggest subject matter relating to the expressed sub-set-size gene, and relies upon Chtioui as allegedly disclosing this subject matter, identifying Chtioui's "binary chromosomes with values 0 and 1 used for crossover in evolving populations [as meeting] the claim language". Office Action page 11.

Applicants respectfully traverse.

Both claim 1 and Chtioui relate to selecting a sub-set of features (or measurements) from a larger set of features (or measurements) for use in a classifier. However, the approach employed by Chtioui is quite different from that of claim 1.

Chtioui employs chromosomes comprising *binary* genes, in which a value of 1 for the binary gene selects the corresponding feature (and, presumably, 0 indicates the corresponding feature is not selected). Chtioui p. 79 right column bottom section. The size of each chromosome is thus equal to the number of available features. *Id.* The genetic algorithm (GA) of Chtioui then evolves these chromosomes comprising binary genes to select the features for use in the classifier. Both the number and identity of the selected features can thus evolve as the number and locations of 1 and 0 values in the chromosomes evolves.

Claim 1 employs a very different approach. As recited in claim 1, each chromosome has a set of genes specifying a sub-set of an associated set of measurements. But unlike Chtioui, each gene of the set of genes contains an *index value* which *indexes* a measurement of the associated set of measurements. These genes of claim 1 are therefore not *binary* genes, but rather are index values. Each chromosome of claim 1 also has an expressed sub-set-size gene having a value distinguishing expressed and unexpressed genes of the set of genes of the chromosome. Chtioui has no analog to this sub-set-size gene. Rather, in Chtioui the (binary) value of the gene itself selects (or "de"-selects) the measurement, while the measurement is designated by the *location* of the gene in the chromosome.

This has implications in terms of scalability to a large set of measurements (where a genetic algorithm approach is most likely to be practical). In an illustrative example, the set of measurements includes 10,000 measurements (present application p. 7 lines 8-13) and the set of genes includes 15 genes specifying 15 measurements (the total chromosome has 16 genes including the expressed sub-set-size gene). *Id.* p. 9 lines 25-27. As each index value which may range 0, ..., 9999, each gene must include 14 bits, making the chromosome $14 \text{ bits} \times 15 \text{ genes} + 4 = 214 \text{ bits}$. The "+4" accounts for the expressed sub-set-size gene assuming here the expressed sub-set-size gene stores an ordinal position (e.g., claim 2) and with 15 genes the ordinal position is no larger than 15. (An alternative "binary mask" embodiment, e.g. present application page 10 line 28 to page 11 line 3, would have a 15 bit expressed sub-set-size gene leading to a 225 bit chromosome.)

Now compare this with Chtioui, which does not have an expressed sub-set-size gene having a value distinguishing expressed and unexpressed genes of the set of genes of the chromosome. Instead, Chtioui has one (binary) gene for each measurement, leading to 10,000 genes encompassing 10,000 bits in the illustrative case of 10,000 available measurements. In general, Chtioui employs a chromosome *of size equal to the number of available features* and comprising genes containing *binary selection values* with one bit corresponding to each available feature. This is over 40 times larger than the gene of claim 1, which adversely impacts scalability.

Furthermore, each Chtioui chromosome corresponds to an *extremely sparse* binary vector, whose sparsity increases with increasing number of available measurements. For example, if 10 measurements are ultimately selected for use in classification, then the optimized Chtioui chromosome includes 10 "1" bits and 9,990 "0" bits. Mutation probabilities are also very low, e.g. of order $1/10,000 = 10^{-4}$. A substantially higher mutation probability would convert too many of the 9,990 "0" bits to "1" bits. By way of illustrative example, given a chromosome with 10 "1" bits and 9,990 "0" bits, a mutation rate of as low as 5% would convert about $9,990 \times 0.05 \cong 500$ of the "0" bits to "1" bits in a single generation.

In contrast, each chromosome of claim 1 is only 214 bits, and corresponds to only 16 genes and at most 15 measurements. Mutation probabilities can be high since the mutation of a gene of the set of genes merely chooses a different measurement, *without* impacting the *number* of selected measurements. The number of selected chromosomes *also* evolves in accordance with claim 1, but through the evolution of the *separate expressed sub-set-size gene*. This approach scales well to a large set of available measurements (e.g., 10,000 or more) from which a small number of measurements (e.g., about 10) are to be selected for use in the classifier.

Ooi cannot remedy these deficiencies of Chtioui. Ooi discloses a chromosome in which each gene contains an index value which indexes a measurement of the associated set of measurements. Ooi p. 39 1st column (heading “String Representation”). Ooi also discloses using only the first R genes out of R_{max} genes in the string for use in classification. *Id.* However, there is no suggestion in Ooi of *adding an additional gene* specifying R and *evolving that added gene* to optimize the number of features used in the classification.

Moreover, the skilled artisan reading both Ooi and Chtioui *and* desiring to optimize the number of features used in classification would *still* not be motivated toward claim 1. Rather, the skilled artisan reading both Ooi and Chtioui would be motivated toward the solution disclosed in Chtioui of using a *binary-valued* chromosome of *size equal to the number of available features*. Nothing in the Ooi or Chtioui reference would fairly suggest the very *different* solution of claim 1.

Claim 2 depends from claim 1, and recites the set of genes of each chromosome define an ordered set of genes, and the expressed sub-set-size gene contains an *ordinal position value* separating the expressed and unexpressed genes in the ordered set. The Office Action appears to identify Chtioui’s binary values as “ordinal position values” – they are *not* ordinal position values (that is, selecting a *position* in an ordered list or set), they are *selection* values that select (or do not select) corresponding features for use in the classifier.

Claim 9 depends from claim 1, and recites (among other subject matter) replacing a selected chromosome of the present generation chromosome population with a selected offspring chromosome *if either*: (i) the selected offspring chromosome is more fit than the selected chromosome of the present generation chromosome population, *or* (ii) the selected offspring chromosome is *as fit* as the selected chromosome of the present generation chromosome population *and the selected offspring chromosome has fewer expressed genes* than the selected chromosome of the present generation chromosome population.

In Ooi, the number of expressed genes is R , which is not evolved. Accordingly, condition (ii) can never arise. In Chtioui the number of selected features equals the number of genes having value “1”, which does evolve. However, Chtioui’s selection process (page 79 left column, #3 and #4) does not fairly suggest any dependency of the chromosome selection on the number of genes having value “1”.

Claim 15 recites (among other subject matter) generating offspring chromosomes from parent chromosomes of the present chromosome population by: (i) filling genes of the offspring chromosome with gene values common to both parent chromosomes and (ii) filling remaining genes with gene values that are unique to one or the other of the parent chromosomes. The Office Action acknowledges that Ooi does not disclose or fairly suggest this subject matter (Office Action page 10), and identifies element (i) in Chtioui (*Id.* page 11).

Respectfully, however, Chtioui does not disclose element (ii). The binary-valued genes of Chtioui have only two possible gene values: “1” or “0”. Assuming that each chromosome selects at least one available measurement, it follows that each Chtioui chromosome includes *both* gene values of 1 and 0. Thus, there is no such thing as a gene value that is *unique* to one or the other of the parent chromosomes.

Claim 15 further recites selectively mutating genes values of the offspring chromosomes that are unique to one or the other of the parent chromosomes without mutating gene values of the offspring chromosomes that are common to both parent chromosomes. The Office Action does not identify this limitation in either Ooi or

Chtioui. Still further, the mutation process of Chtioui (p. 79 #6) does not mention parental source information as input for performing mutations.

As noted in the present application (*not* Ooi and *not* Chtioui), the approach of claim 15 in which common genes are maintained is advantageous at least in that it promotes propagation of these common genes. Present application p. 12 lines 2-5.

Claim 16 depends from claim 15, and recites wherein a mutation rate for the selective mutating of the gene values that are unique to one or the other of the parent chromosomes is greater than 5%. The Office Action argues this would have been obvious since Ooi discloses mutation rates of up to 0.02% (Office Action page 12).

Respectfully, the *lower* 5% threshold of claim 16 is *250 times larger* than the *uppermost* 0.02% rate of Ooi. Moreover, as already pointed out in discussing claim 1, mutating the sparse binary-valued chromosomes of Chtioui at high mutation rates makes it difficult or impossible to maintain sparsity sufficient to select a reasonable number of measurements (e.g., a few measurements) from a set of thousands or tens of thousands (or more) available measurements. This observation is expressly (albeit qualitatively) confirmed in Chtioui itself, which states the mutation probability “usually has a very low value”. Chtioui page 79 #6.

Claim 19 recites (among other subject matter) computationally genetically evolving the genes of the chromosomes to produce successive generation chromosome populations, the producing of each successor generation chromosome population including: *introducing a selected level of simulated noise into values of the set of measurements for a group of subjects*, generating offspring chromosomes by mating chromosomes of the present chromosome population, selectively mutating genes of the offspring chromosomes, and *updating the chromosome population with offspring chromosomes based on a fitness of each chromosome determined respective to the values of the measurements of the group of subjects with the introduced simulated noise*.

The rejection of claim 19 (Office Action pages 8-12) does not appear to mention noise *at all*, much less identify disclosure of introduction of simulated noise as recited in claim 19. Applicants respectfully request that the forthcoming Office

Action either identify the subject matter of claim 19 in the proposed combination of Ooi and Chtioui, or withdraw the rejection of claims 19-20.

The present application (*not* Ooi and *not* Chtioui) disclose the following rationale for adding simulated noise:

The introduction of simulated noise counteracts possible fitting of the classification functions to correlations of measurement errors. For example, if the measuring instruments systematically read slightly high when the cancer cases were measured and slightly low for the cancer-free cases, the genetic evolving may converge onto these systematic error patterns. The optional introduction of simulated noise by the cross-validation and noise-adding algorithm 24 perturbs the measurements for each generation of the evolutionary search.

Present application page 18 lines 11-17.

Claim 21 is amended to incorporate the subject matter of canceled claim 25, and recites (among other subject matter) evolving *a number of expressed genes in each chromosome* and employing a fitness criterion evaluated without reference to unexpressed genes of each chromosome, and selecting chromosomes that survive into each successive generation *using a selection criterion biased toward selecting chromosomes having a smaller number of expressed genes over chromosomes having a larger number of expressed genes*.

The Office Action does not articulate any basis for rejecting claim 25 (again, claim 21 as amended has scope commensurate with claim 25). It appears that the Office Action acknowledges that Ooi does not disclose or fairly suggest evolving a number of expressed genes in each chromosome – indeed, to the contrary, Ooi discloses having a *fixed number R* of expressed genes in each chromosome. *See* Ooi p. 39 1st column (heading “String Representation”). Chtioui does disclose evolving a number of expressed genes in each chromosome (insofar as the number of selected features, that is, the number of binary gene values equal to “1”, evolves). However, the selection criterion of Chtioui described at page 79 left column (#4) is based entirely on the value of the fitness function, with no fair suggestion of biasing toward selecting chromosomes having a smaller number of expressed genes.

As with claim 19, Applicants respectfully request that the forthcoming Office Action either identify the subject matter of claim 21 in the proposed combination of Ooi and Chtioui, or withdraw the rejection.

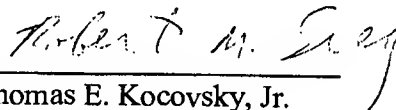
Finally, Applicants remind the Office of the potential for rejoinder of withdrawn claims 3, 4, 7, 8, 21, and 22 directed to unelected species, as per 37 C.F.R. § 1.141, upon allowance of any base claim, and urge reinstatement and consideration of any of claims 3, 4, 7, 8, 21, and 22 upon allowance of a base claim from which it depends.

In view of the foregoing, Applicants urge reconsideration and allowance of claims 1-24 and 26 as set forth herein.

CONCLUSION

In view of the foregoing, Applicants urge allowance of all claims 1-24 and 26. In the event personal contact is deemed advantageous to the disposition of this case, the Examiner is requested to telephone the undersigned at 216.363.9000.

Respectfully submitted,



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